Response to Office Action Summary
Application No. 10/686,374
Applicant: Savva, Michalakis
Examiner: Gollamudi S. Kishore, Ph.D.

1. Claim 1 was amended appropriately to claim the only cationic lipids with carbamate linkages depicted in Formula S and the synthesis of which was demonstrated in multiple examples. Also, an additional example was added (example 14) to describe the synthesis of primary ammonium analogs of formula S.

2. Claim 2 was cancelled and other dependent claims were added.

3-4. The instant cationic compounds disclosed the pending application 10/686,374 are indeed described in US patent, 6,268,516 by Schneider et al.. However, the reasons cited alphabetically below suggest that the patent US6,268,516 is without merit with respects to the structures described in pending application 10/686,374:
A. None of the Examples and synthetic schemes describes the synthesis of the structures described in the pending application 10/686,374.
B. Unlike the easy synthesis of cationic lipids demonstrated in the Examples of US6,268,516, the starting material for the synthesis of Structure S lipids is not commercially available. It is therefore highly plausible that Schneider et al., have never synthesized any of the Structure S cationic lipids.
C. None of Figures describes application of the structure S cationic lipids in gene therapy.
E. Structure S cationic lipids have unique physicochemical properties. None of these properties is shared with the lipids described in Examples and Figures of US6,268,516 or any other 1,2-double-chained cationic derivatives, in general.
F. Cationic Lipids that bear the polar head group described in the pending application 10/686,374, are fluid and elastic at physiological temperature, they are pH-sensitive and they don't require the presence of helper lipids to mediate cell transfection. Contrary to that, all Figures described in US6,268,516 show very clearly that all cationic lipids required the presence of DOPE (helper lipid) to mediate transfection.

A recent publication in Biophysical Chemistry describes some of the above (Spelios et al., Effect of spacer attachment sites and pH-sensitive headgroup expansion on cationic lipid-mediated gene delivery of three myristoyl derivatives. *Biophysical Chemistry.* Accepted for publication 05/22/2007. Article in Press.

5. The compounds claimed in pending application No. 10/686,262 are 1,2-diaminopropyl-3-carbamoyl derivatives whereas the compounds described in copending application 10/686,374 are 1,3-diaminopropyl-2-carbamoyl analogs. Thus, there is no issue of double patenting.

AMENDMENT DOCUMENT

A. Application No. 10/686,374
Applicant: Savva, Michalakis
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